

**I. REMARKS**

Claims 1, 7-22, 24, 32, 34, 35, and 39-45 are pending. Claims 33-35 are withdrawn. The final Office Action dated July 17, 2007, has been received and carefully noted. The enclosed Declaration, the enclosed one-month Petition for Extension of Time, and the following remarks are being submitted as a full and complete response thereto. No amendments to the specification or claims are made at this time.

Entry of the Declaration is proper under 37 C.F.R. § 1.116 since the Declaration: (a) places the application in condition for allowance for reasons discussed herein; (b) does not raise any new issue regarding further search and/or consideration since the Declaration amplifies issues previously discussed throughout prosecution; and (c) places the application in better form for appeal, should an appeal be necessary. Entry of the Declaration is thus respectfully requested.

Claims 1, 7-22, 24, and 39-45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Del Soldato et al. (WO 95/30641) in view of Lai et al. (U.S. Patent No. 6,355,666), Cainelli et al. (J. Chem. Soc. Perkin. Trans. (1987) 2637-2642) and Hwu et al. (Synthesis (1994) 471-474). This rejection is traversed.

Applicants again agree with the Examiner that "Del Soldato et al. do not teach the reaction of diclofenac with a glycol linker, reaction of that product with an alkylsulfonyl source, or reaction with an alkali nitrate. Also, the exact details of the solvent, purification, and other parameters provided in dependent claims are not addressed" (Office Action, page 5). However, Applicants respectfully maintain that Lai et al., Cainelli

et al., and Hwu et al., alone or in combination, do not satisfy the deficiencies of Del Soldato et al.

Applicants respectfully maintain that lowering the reaction temperature of the cited references to the maximum temperature of 90°C of step (3) of present claim 1 would not have been obvious to those of skill in the art in view of the cited references, much less the result of routine optimization. As previously discussed, the cited references teach away from the claimed temperature. In particular, Hwu et al. discloses that the % yield of nitrate esters from the corresponding alkyl toluenesulfonates decreases with a decrease in reaction temperature (see the Table on page 471 disclosing the lowest 67% percent yield at 110°C). As such, those of skill in the art would not have been motivated by Hwu et al. to decrease the reaction temperature, as a decreased % yield would have been expected.

Further, the enclosed Declaration demonstrates that the reaction temperature does not significantly affect the percentage of conversion of a sulfonate intermediate as disclosed in Hwu et al., but that an increase in reaction temperature increases the formation of impurities. As such, the nitration step (corresponding to step (3) of claim 1) should be run at a temperature lower than 90°C, as claimed, to avoid the formation of an unacceptable amount of the impurities, such as impurity (Va). Moreover, as noted in the Declaration, the formation of impurity (Va) could not be forecast on the basis of the results of laboratory scale experiments because the increase of impurities could not be detected at lab scale, but could be detected only during the scale up to a larger (5L)

reactor. Accordingly, varying the reaction temperature cannot be considered a matter of routine optimization to be accomplished by conducting simple experimental testing.

Thus, the disclosure of Hwu et al. may not be combined with the other cited references to obtain the presently claimed invention and it would not have been the result of routine optimization for those of skill in the art to decrease the reaction temperature, much less to obtain the unexpected results of the presently claimed invention.

Further, Cainelli et al. and Lai et al. do not satisfy the deficiencies of Hwu et al. and Del Soldato et al. Cainelli et al. discloses conversion of mesylate derivatives to the correspondent nitrates by treatment with tetrabutylammonium nitrate in toluene at reflux (i.e., at toluene's boiling point of 110°C) (Cainelli et al., page 2640, left column, third full paragraph, and page 2641, left column, fourth full paragraph). Meanwhile, Lai et al. merely discloses the preparation of a sulfonate intermediate and does not seem to disclose conversion of the sulfonate derivative to a NO-donating compound, much less at the low temperature of the presently claimed invention. Lai et al. does not make up for the deficiencies of the other references.

As none of the cited references, alone or in combination, teach or suggest all of the elements of the presently claimed invention, Applicants submit that the presently claimed invention would not have been obvious to those of skill in the art, much less the unexpected advantages thereof. Accordingly, for at least the above reasons, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 7-22, 24, and 39-48 under 35 U.S.C. § 103(a) over Del Soldato et al. in view of Lai et al., Cainelli et al. and Hwu et al.

## II. CONCLUSION

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

In the event that this paper is not being timely filed, the Applicants respectfully petition for an appropriate extension of time. Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to Counsel's Deposit Account Number 01-2300, referencing Docket Number 026220-00064.

Respectfully submitted,

  
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Enclosures: Declaration  
Petition for Extension of Time (one month)